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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,190	02/28/2002	Pia M. Challita-Eid	511582003420	7796

36327 7590 08/03/2005

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EXAMINER

BLANCHARD, DAVID J

ART UNIT	PAPER NUMBER
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1643

DATE MAILED: 08/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/087,190	Applicant(s) CHALLITA-EID ET AL.	
	Examiner David J. Blanchard	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4, 6, 7, 9, 10, 12, 13, 15, 48, 49, 54 and 78-82 is/are pending in the application.
- 4a) Of the above claim(s) 15, 48, 49 and 54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4, 6-7, 9-10, 12-13 and 78-82 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Exhibit A</u> |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06 July 2005 has been entered.

2. Claims 1-3, 5, 8, 11, 14, 16-47, 50-53 and 55-77 are cancelled.

Claims 4, 6 and 12 have been amended.

Claims 15, 48-49 and 54 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

3. Claims 4, 6-7, 9-10, 12-13 and 78-82 are under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

6. The objection to the specification for containing embedded hyperlinks and/or other form of browser-executable code is withdrawn in view of the amendments to the specification.

7. The rejection of claims 4-7, 9-10, 12-13 and 78-82 under 35 U.S.C. 102(e) as being anticipated by Tang et al is withdrawn in view of the amendments to the claims.

8. The rejection of claims 4-7, 9-10, 12-13 and 78-82 under 35 U.S.C. 102(e) as being anticipated by Edwards et al is withdrawn in view of the amendments to the claims.

9. The rejection of claims 4-7, 9-10, 12-13 and 78-82 under 35 U.S.C 103(a) as being unpatentable over Edwards et al in view of Thorpe et al is withdrawn in view of the amendments to the claims.

New Grounds of Rejections

10. Claims 4, 6-7, 9-10, 12-13 and 78-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The response filed 7/6/2005 has introduced NEW MATTER into the claims. The claims previously drawn to antibodies or fragments thereof that specifically bind SEQ ID NO:3 are presently amended to recite isolated monoclonal antibodies or fragments thereof raised against a fragment of SEQ ID NO:3 comprising at least 5 amino acids of a peptide selected from amino acid residues 1-67, 78-169, 178-205, 1-22, 117-142, 21-57, 76-113 and 120-149 of SEQ ID NO:3, wherein the monoclonal antibodies or

fragments thereof specifically bind SEQ ID NO:3. Thus, as presently amended, the claims recite antibodies that specifically bind particular epitopes within the SEQ ID NO:3. Applicant's response filed 7/6/2005 states that presently claimed amino acid residues 1-67, 78-169 and 178-205 of SEQ ID NO:3 are supported by Figure 5A, amino acid residues 1-22 and 117-142 are supported by Figure 6A, amino acid residues 21-57, 77-113 and 120-149 are supported by Figure 7A and the amino acid residues 178-205 are supported by Figure 8A and support for selecting these regions is found at page 14, line 32 through page 15, line 16 of the specification. The as-filed Figures and the specification as pointed to by applicant do not provide adequate written support for the presently claimed antibodies raised against and hence, specific to particular epitopes of SEQ ID NO:3. The as-filed Figures as pointed to by applicant merely characterize the polypeptide of SEQ ID NO:3 (i.e., 121P1F1) by hydrophilicity, hydrophobicity, percent accessible residues and average flexibility profiles (Figs. 5A, 6A, 7A, and 8A, respectively). Further, the specification as pointed to by applicant does not appear to be the originally filed specification. Upon review of the instant application, the relevant text as pointed to by applicant is found at page 17 line 25 through page 18, line 15 and page 18, line 29 of the originally filed specification, filed 2/28/2002. The specification as pointed to by applicant refers to the selection of the peptides based on the profiles of Figs. 5A-8A in the context of HLA or cellular immune response vaccine compositions that contain or encode one or more peptides of 121P1F1 (i.e., SEQ ID NO:3), not in the context of raising antibodies to these particular epitopes (see page 15, beginning at line 33). Although the Figures appear to provide a criteria for selecting peptides of SEQ ID

NO:3, they do not identify the specific regions of SEQ ID NO:3 with respect to antibody production nor do they provide sufficient written description to lead one skilled in the art to produce a monoclonal antibody to a fragment of SEQ ID NO:3 comprising at least 5 amino acids of a peptide selected from amino acid residues 1-67, 78-169, 178-205, 1-22, 117-142, 21-57, 76-113 and 120-149 of SEQ ID NO:3. In re Ruschig, 379 F.2d 990, 154 USPQ 118 (CCPA 1967) makes clear, one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say here is my invention. In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure. See id. at 994-95, 154 USPQ at 122; Fujikawa, 93 F.3d at 1570-71, 39 USPQ2d at 1905; Martin v. Mayer, 823 F.2d 500, 505, 3 USPQ2d 1333, 1337(Fed. Cir. 1987) (It is `not a question of whether one skilled in the art might be able to construct the patentee's device from the teachings of the disclosure. ... Rather, it is a question whether the application necessarily discloses that particular device.') (quoting Jepson v. Coleman, 314 F.2d 533, 536, 136 USPQ 647, 649-50(CCPA 1963)). In the instant case, the disclosure pointed to by applicant, which provides guidance for selecting peptides in the context of HLA or cellular immune response vaccine compositions and the Figures would not have necessarily led one skilled in the art to select the particular regions of SEQ ID NO:3 or fragments thereof for raising antibodies as recited in the presently amended claims. Thus, the specification and Figures 5A-8A do not provide adequate written support for antibodies raised against a fragment of SEQ ID NO:3 comprising at least 5 amino acids of a peptide selected from amino acid residues 1-67, 78-169, 178-205, 1-22, 117-142,

21-57, 76-113 and 120-149 of SEQ ID NO:3 and in turn, antibodies that bind SEQ ID NO:3 at an epitope comprising at least 5 amino acids of a peptide selected from amino acid residues 1-67, 78-169, 178-205, 1-22, 117-142, 21-57, 76-113 and 120-149 of SEQ ID NO:3. The presently amended claims now recite limitations, which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the presently amended claims, which did not appear in the specification, as-filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in the presently amended claims in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

Applicant is reminded that obviousness is not the standard for the addition new limitations to the disclosure as-filed. It is noted that entitlement to a filing date does not extend to subject matter, which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

11. Claims 4, 6-7, 9-10, 12-13 and 78-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al (WO 01/53312 A1, 1/21/2000, pp. 1-104, 293, 604-607, previously cited on PTO-892 mailed 11/15/2004) in view of Harlow et al (Antibodies, A Laboratory Manual, Chapter 5, pp. 75-76, 1988).

The claims are drawn to an isolated monoclonal antibody or fragment thereof that

binds to SEQ ID NO:3, wherein the antibody is raised against a fragment of SEQ ID NO:3 selected from amino acid residues 1-67, 78-169, 178-205, 1-22, 117-142, 21-57, 76-113 and 120-149 of SEQ ID NO:3, wherein said antibody or fragment thereof is conjugated to an agent, is a monoclonal antibody, a human antibody, a humanized antibody or a chimeric antibody and wherein the antibody fragment is a Fab, F(ab)₂, Fv or sFv fragment. Further, the claims recite that the monoclonal antibody is recombinantly produced and is a single-chain antibody. Claim 78 recites wherein the agent is a diagnostic agent or a cytotoxic agent and claims 79-82 recite various radioactive isotopes, chemotherapeutic agents and toxins. Claim 12 is drawn to a hybridoma that produces said monoclonal antibody that binds to SEQ ID NO:3.

Tang et al teach a polypeptide (SEQ ID NO:3188) having 100% amino acid identity with residues 16-205 of SEQ ID NO:3 and monoclonal antibodies to the polypeptide, which can be raised using a peptide fragment of the polypeptide that comprises at least 6 amino acid residues (see pages 74-84 and 293 and the alignment attached to the back of this Office Action; Exhibit A). Tang et al teach human, humanized, single-chain antibodies and antibody fragments including Fab, F(ab)₂ and Fv fragments (see pages 76 and 78-80). Tang et al teach monoclonal antibodies produced by recombinant DNA methods (i.e., recombinantly produced) as well as by hybridomas (see page 77, lines 23-24 and page 76). Tang et al also teach immunoconjugates comprising an antibody conjugated to a cytotoxic agent or diagnostic agent, wherein the cytotoxic agent is a chemotherapeutic agent, a toxin or a radioactive isotope (see page 83, lines 32-35). Tang et al teach toxins including diphtheria toxin,

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enomycin, phenomycin, Pseudomonas exotoxin A, abrin A chain, mitogellin, modeccin A chain and alpha-sarcin as well as the chemotherapeutic agent gelonin (see page 84, lines 2-7) and radioactive isotopes including ^{212}Bi , ^{131}I , ^{90}Y and ^{186}Re . Tang et al do not specifically teach the regions of SEQ ID NO:3 used for raising a monoclonal antibody to SEQ ID NO:3. This deficiency is made up for in the teachings of Harlow et al.

Harlow et al teach that the smallest peptide that will consistently elicit antibodies that bind the original protein are 6 residues in length (see page 76) and both the N- and C-terminal residues of a polypeptide are often exposed and can be targeted for producing anti-peptide antibodies that will bind the native protein (see pages 75-76).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced monoclonal antibodies and hybridomas producing said monoclonal antibodies to the N and C-terminal regions of the polypeptide of SEQ ID NO:3188 taught by Tang et al by the method of Harlow et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced monoclonal antibodies and hybridomas producing said monoclonal antibodies to the N and C-terminal regions of the polypeptide of SEQ ID NO:3188 taught by Tang et al by the method of Harlow et al because Tang et al teach monoclonal antibodies and hybridomas producing said monoclonal antibodies as well as antibody conjugates to the polypeptide of SEQ ID NO:3188 (identical to amino acid residues 16-205 of SEQ ID NO:3; see Exhibit A attached to the back of this Office Action) as well as raising antibodies against the full length protein using peptide fragments of the protein that are at least 6 amino acids in

length and Harlow et al teach that both the N- and C-terminal residues of a protein are often exposed and useful as immunogen for producing anti-peptide antibodies that will bind the native protein. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated and had a reasonable expectation of success to have produced monoclonal antibodies and hybridomas producing said monoclonal antibodies against SEQ ID NO:3188 that are raised against an N-terminal or the C-terminal peptide of SEQ ID NO:3188 that is at least 6 amino acid residues in length because Tang et al specifically suggests producing antibodies to the protein using peptide fragments that are at least 6 amino acids in length as immunogen and Harlow teaches that both the N- and C-termini are exposed and suitable for producing anti-peptide antibodies that will bind the native protein and according to Harlow a significantly high percentage of antibodies raised against a C-terminal peptide will bind the native protein, indicating a reasonable expectation of success. One of ordinary skill in the art would reasonably conclude that the monoclonal antibodies and hybridomas produced according to Tang et al and Harlow et al also possesses the same structural and functional properties as those of the antibodies and hybridomas claimed and, therefore, it appears that Tang et al and Harlow et al have produced monoclonal antibodies an hybridomas that are identical to the claimed monoclonal antibodies and hybridomas because a monoclonal antibody raised against an N-terminal or C-terminal peptide of at least 6 amino acids in length of SEQ ID NO:3188 would necessarily bind the identical peptide of SEQ ID NO:3 found within N-terminal residues 16-67 of SEQ ID NO:3 or found within C-terminal residues 178-205 of SEQ ID NO:3 since the amino acid

sequences are identical (i.e., SEQ ID NO:3188 is identical to residues 16-205 of SEQ ID NO:3; Exhibit A). Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed monoclonal antibodies and hybridomas with the monoclonal antibodies and hybridomas of Tang et al and Harlow et al, the burden of proof is upon Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed monoclonal antibodies and hybridomas and the monoclonal antibodies and hybridomas of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusions

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature, matching or

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filed papers or relating to the status of this application or proceeding should be directed to Tony Parks for Art Unit 1643 whose telephone number is 571-272-0543.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827



LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

Exhibit A

RESULT 3
 AAM40043
 ID AAM40043 standard; protein; 190 AA.
 AC AAM40043;
 DT 23-OCT-2001 (first entry)
 DE Human polypeptide SEQ ID NO. 3188.
 XX Human; nocotropic; immunosuppressant; cytostatic; gene therapy; cancer;
 XX peripheral nervous system; neuropathy; central nervous system; CNS;
 XX Alzheimer's; Parkinson's disease; Huntington's disease; haemostatic;
 XX amyotrophic lateral sclerosis; Shy-Drager Syndrome; chemotactic;
 XX chemokine; thrombolytic; drug screening; arthritis; inflammation;
 XX leukaemia.
 OS Hemo spleen.
 XX
 XX MO300153312-A1.
 XX
 XX 26-JUL-2001.
 XX
 XX 26-DEC-2000; 2000MO-DS034263.
 XX
 XX 23-DEC-1999; 99US-00471275.
 XX 21-JAN-2000; 2000US-00488725.
 XX 25-APR-2000; 2000US-00552317.
 XX 20-JUN-2000; 2000US-00598042.
 XX 19-JUL-2000; 2000US-00620313.
 XX 03-AUG-2000; 2000US-00653450.
 XX 14-SEP-2000; 2000US-00662191.
 XX 19-OCT-2000; 2000US-00693036.
 XX 29-NOV-2000; 2000US-00727344.
 XX
 XX (HYSB-) HYSBO INC.

PI Tang YT, Liu C, Aouni V, Chen R, Ma Y, Qian XB, Ren P, Wang D,
 PI Wang J, Wang Z, Wehrman T, Xu C, Xue AJ, Yang Y, Zhang J, Zhao Q;
 PI Zhou P, Goodrich R, Drmanac RT;
 XX WPI; 2001-442253/47.
 DR N-PSDB; AA159199.
 XX
 PT Novel nucleic acids and polypeptides, useful for treating disorders such
 PT as central nervous system injuries.
 XX
 XX Example 4; SEQ ID NO 3188; 10078pp; English.
 CC The invention relates to human nucleic acids (AA157798-AA161369) and the
 CC encoded polypeptides (AAM38642-AAM42213) with nocotropic,
 CC immunosuppressant and cytostatic activity. The polynucleotides are useful
 CC in gene therapy. A composition containing a polypeptide or polynucleotide
 CC of the invention may be used to treat diseases of the peripheral nerve
 CC system, such as peripheral nervous injuries, peripheral neuropathy and
 CC localised neuropathies and central nervous system diseases, such as
 CC Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic
 CC lateral sclerosis, and Shy-Drager Syndrome. Other uses include the
 CC utilisation of the activities such as: immune system suppression,
 CC Actin/limbin activity, chemotactic/chemokinetic activity, haemostatic
 CC and thrombolytic activity, cancer diagnosis and therapy, drug screening,
 CC assays for receptor activity, arthritis and inflammation, leukaemia and
 CC C.N.S disorders. Note: The sequence data for this patent did not form
 CC part of the printed specification
 XX
 SQ Sequence 190 AA;

Query Match 93.1%; Score 975; DB 4; Length 190;
 Best Local Similarity .100.0%; Pred. No. 6e-82;
 Matches 190; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 16 MEETPSKQVFOLEKIAPEKGTMSKGTOSTVNDGMDPDERICTNTYMAAP 75
 DB 1 MEETPSKQVFOLEKIAPEKGTMSKGTOSTVNDGMDPDERICTNTYMAAP 60
 QY 76 SGLHARKHLEVLVESQLSFGSKANSLQKSTIEKXIGRCTBERTLALSLSDRE 135
 DB 61 SGLHARKHLEVLVESQLSFGSKANSLQKSTIEKXIGRCTBERTLALSLSDRE 120
 QY 136 QLKAEVETKDCDPQVVEIRQANKVANEANRWTDNIFALKSNKXKGFEEKXIDRTF 195
 DB 121 QLKAEVETKDCDPQVVEIRQANKVANEANRWTDNIFALKSNKXKGFEEKXIDRTF 180
 QY 196 GIPEDPDYID 205
 DB 191 GIPEDPDYID 190